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- **SCANDINAVIAN JOURNAL OF PRIMARY HEALTH CARE vol. 7, no. 1, 1989, STOCKHOLM pages 23 - 26 GADE J. ET AL 'Paraghurt for patients with irritable bowel syndrome'**
- **BIOLOGICAL ABSTRACTS vol. 79, no. 2 , 1985, Philadelphia, PA, US; abstract no. 14131, WADSTROM T. ET AL 'Streptococcus faecium M-74 in control of diarrhea induced by a human enterotoxigenic Escherlquia coli strain in an infant rabbit model' page AB-544 ;**
- **BERGEY'S MANUAL OF SYSTEMATIC BACTERIOLOGY, VOL. 2, 1986, pages 1046 and 1063-1064**

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Important embodiments of the invention are:

1. An edible composition comprising viable organisms of strain NCIMB 40371, packaged with instructions recommending a mode of administration to a human patient exhibiting symptoms of gastroenteric disorder;

2. a controlled diet for a human patient exhibiting symptoms of IBS, including such a composition;

3. a method of alleviating symptoms of gastroenteric disorder, specially IBS in a human patient by the oral administration of an edible composition comprising viable organisms of strain NCIMB 40371, the composition being administered in an amount sufficient to establish and/or maintain a population of said strain in the gastroenteric tract of said human patient; and

4. a method of alleviating symptoms of IBS in a human patient by the repeated administration of a fermented milk product containing viable organisms of strain NCIMB 40371.

Irritable bowel syndrome (IBS)

Although individuals later diagnosed as suffering from IBS form a very large proportion of the patients seen by gastroenterologists (20-50%) there are no simple tests to confirm the diagnosis. However the symptoms most frequently associated with the condition are:-

1. Abdominal pain relieved by bowel movement
2. Loose stools associated with the pain
3. More frequent stools associated with the pain
4. Abdominal distension
5. Mucus in the stool
6. A sense of incomplete evacuation (Manning et al, 1978)

If no other organic disorder can be found to account for the above symptoms the diagnosis is usually IBS.

As well as the recognised colonic symptoms listed above there may be additional extracolonic symptoms associated with the disease, these include chronic headache or migraine and swelling and pain in the joints (Tilbe & Sullivan, 1990; Watson et al, 1978).

The individuals seen and diagnosed as IBS cases by clinicians may only represent 'the tip of the iceberg'. Epidemiological surveys in the UK, the USA and Denmark showed that 14%, 17% and 15% respectively of apparently healthy individuals had experienced more than 6 episodes of lower abdominal pain with at least 3 of the typical six IBS symptoms during the previous year: Drossman et al (1982), Krag (1985), Thompson and Heaton (1980). So only a minority of individuals with IBS (presumably the more severe cases plus individuals prone to seek medical advice on all possible occasions) go to their doctors with the problem. The majority of the sufferers either put up with it or try assorted home remedies, most of which are unproven and probably useless.

Causes of IBS symptoms

Individuals suffering from IBS experience disturbances in the motility of both the upper and lower gut, and these can lead to diarrhoea and/or constipation and pain. The abnormal gut function could be due to a disturbance of intestinal control. The extracolonic manifestations of the syndrome, such as chronic headache and migraine, imply that an agent acting systemically could also be involved (Watson et al 1978).

It has been suggested that prostagladin E2 (PGE) may act as a intestinal mediator in the diarrhoeal form of IBS. Exogenous PGE exerts a potent secretory effect on the intestinal epithelium and can evoke copious watery diarrhoea in humans following oral, intrajejunal or parenteral administration. PGs also affect intestinal motility. PGE is synthesized locally in the small intestine and its synthesis/release is normally under hormonal and neutral control. Abnormal release of PGE would clearly give rise to adverse symptoms and individuals with IBS-diarrhoea often do have higher than normal PGE levels (Rask-Madsen & Bukhave, 1985). One condition that may trigger the release of PGE is food intolerance. Jones et al (1982) reported that specific foods provoked symptoms of IBS in 14/21 patients and this was associated with increased levels of rectal PGE.

Many patients can date the onset of their IBS to a definite event such as a bout of gastroenteritis, abdominal or pelvic surgery, or a course of antibiotics. Women undergoing hysterectomy are far more likely to develop IBS symptoms post-operatively if they are given metronidazole following the operation. This indicates that if the gut flora is disturbed a new gut ecosystem may gain dominance that makes the patient more prone to IBS (Hunter and Jones, 1985). A

chronic infection with a hitherto unidentified pathogen or enteroadherent E.coli has been suggested as the course of IBS and inflammatory bowel disease in a proportion of patients (Borody et al, 1989; Burke and Axon, 1988) but another possibility is that the stressed gut can be colonised by bacteria which are harmless generally but can metabolize certain foodstuffs to give intermediates which can trigger PGE release.

Probiotic therapy can benefit IBS patients, but it is necessary to identify a suitable bacterial strain. The mode of action of probiotics is not at present well-understood. The following three parameters seem important.

1. The strain should be a natural intestinal strain, non-pathogenic and non-toxic.

2. A suitable, safe delivery system should be available for giving the patient large numbers of viable cells.

3. The strain should be capable of surviving and metabolizing in the gut environment, e.g. be resistant to low pH and organic acids.

METHODS

Strain and growth media

Strain PR88 is a naturally-occurring gram-positive coccus identified as Streptococcus (Enterococcus) faecium. The API 20S code of the strain is 5357 511 (very good identification Ent.faecium) and it grows on thallous acetate - tetrazolium glucose agar giving white colonies.

PR88 will ferment sugars such as glucose to give acids thereby lowering the pH to about 4.5 and will 'yoghurt' milk media after 19-24 hours at 37°C but the yoghurts used in this study were incubated for 48 hours (a milkintolerant patient was found to react to 24h, but not 48h, yoghurts). Counts of PR88 in the yoghurts were usually between 10^8 and 10^9 per gram and the pH was about 4.6

PR88 was grown in 500 ml aliquots of GYSM* for intracaecal inoculation and 100ml aliquots of DS* for oral inoculation.

*GYSM - 10gm glucose, 3gm yeast extract (Oxoid L21) and 100gm milk powder (Oxoid L31) per litre.

*DS - 10gm glucose and 100gm milk powder (Oxoid L31) per litre.

Batches of set GYSM and 'yoghurts' (individual pots of set DS) were checked to confirm that they were pure cultures of PR88 by plating on blood agar and incubating plates at 37°C both aerobically and anaerobically.

Examination of faecal samples

Faecal samples from the patients were examined before the start of yoghurt therapy and then each week during the trial. The stool samples were first examined microscopically for abnormalities (ova, cysts, parasites, pus cells, red blood cells, mucus etc) and then 'counted' by the method of Miles and Misra (1938) to determine faecal levels of different types of bacteria. The different types of bacteria were enumerated by counting on different selective media and incubating the plates aerobically and anaerobically at 37°C.

This enabled us to determine the viable counts/gm faeces of Ent.faecium, Ent.faecalis, enterobacteria, anaerobes and yeasts. When necessary, preliminary identification was confirmed by microscopy and biochemical tests.

Subjects tested

Seventeen patients with chronic IBS who had previously failed to respond to conventional treatment were selected, and their clinical condition monitored. Nine were 'high volume diarrhoea' (HVD) cases, the remaining eight had intermittent diarrhoea or other IBS symptoms (Table 1).

The average daily faecal weights of the HVD patients were measured (over a period of 3-4 days) before and after treatment. The condition scores of all patients were assessed before and after treatment by the simple index method of Harvey and Bradshaw (1980). In twelve of the patients, the PR88 culture was initially administered by intracaecal intubation and their intestinal PR88 levels were then maintained by daily yoghurts. Five patients had the oral yoghurt therapy only (see Table 1). Later, each individual reduced their yoghurt consumption (one pot every second or third day) until they reached what they considered to be the right frequency to maintain improved health.

By the end of the trial, patients had been treated with PR88 for periods varying from 4 months to 2.5 years.

RESULTS

General bacteriology

The faecal bacteriology of healthy individuals as measured by anaerobe/aerobe ratios can vary considerably from day to day although it is possible to calculate the 'normal range' for faecal samples treated in a standard way.

The faecal bacteriology counts of IBS patients gave a higher percentage of abnormal anaerobe/aerobe ratios than healthy individuals, but after probiotic treatment gave ratios in the normal range. However, the abnormal ratios could be either above or below the norm and many IBS patients gave similar ratios when normal and when in diarrhoeal breakdown. Therefore it can be inferred that although some IBS patients may have an abnormal faecal flora as measured by crude anaerobe/aerobe ratios but there is no characteristic IBS profile. (Imbalances within the aerobe or anaerobe group would not be shown up by this method).

None of the IBS patients had detectable levels of Ent. faecium in their stools before treatment. However many healthy individuals do not appear to carry Ent. faecium either.

The effects of the yoghurt therapy in all 17 patients included in the trial are summarised in Table 2. The therapy was successful in 7/9 HVD patients and in 5/8 of the others. The two failures in the HVD (patients 8 and 9) group reacted adversely to the yoghurts; they were normally intolerant of dairy foods and were clearly affected by some factor in the milk that was not changed by the yoghurting process.

The average daily faecal weights of patients (1) to (7) before and after treatment are given in Table 3; whereas prior to treatment they were high, after treatment they returned to the normal range.

The assessment of the other IBS symptoms was necessarily more subjective than the measurement of faecal weights but it was possible to obtain a 'symptoms index' (method of Harvey and Bradshaw, 1980) from each patient 'before' and 'after' - see Tables 4 and 5. Therapy with strain PR88 reduced the abdominal pain, migraine-like headaches and joint pains associated with IBS in the twelve successful patients and, with the exception of patient (2), these symptoms returned if PR88 therapy was terminated.

DISCUSSION

The public have a conception of yoghurt as a 'health-giving food' but scientific evidence of the beneficial properties of fermented milk products is rather tenuous. One reason for this is that the strains of bacteria used for the commercial production of yoghurt (Lact.bulgaricus and Strep.thermophilus) and other fermented milk products have been selected for rapid growth in vitro and their ability to produce foodstuffs of a pleasant taste. These strains have largely lost the ability to survive in vivo so a probiotic effect with ordinary commercial yoghurts is rather unlikely. However, the Ent. faecium PR88 has the ability to adhere to gut cells and survive in the intestinal environment. PR88 yoghurts milk much more slowly than a commercial culture but it can survive and proliferate in the alimentary tract. Early experiments in patients showed that after intubation, PR88 could implant and maintain large intestinal populations for several weeks. Later experiments showed that yoghurts taken orally could also result in high numbers of the strain in the intestine, as patients in the trial usually had faecal levels of PR88 of 10^6-10^9 per gram.

Probiotic therapy with PR88 was very effective at alleviating the symptoms of IBS, particularly diarrhoea-associated IBS. The average daily faecal weights of the patients were determined before and after probiotic treatment and clearly demonstrated the efficacy of PR88. In 5/7 IBS patients with the diarrhoeal syndrome the average daily faecal weight was brought down to normal levels by probiotic therapy. The two 'failures' were both intolerant of cow's milk and also reacted adversely to dairy yoghurts. The three patients with intermittent diarrhoea also responded well to yoghurt treatment as did 2 individuals with IBS without diarrhoea. The other symptoms of IBS such as abdominal pain, migraine-like headache and arthritic pains and swelling of the joints could also be relieved by the probiotic therapy (see Table 4).

Many (but not all) of the IBS patients were initially given PR88 by intracaecal tube in an attempt to get a rapid improvement in their condition. Intracaecal intubation bypasses the stomach and enables PR88 to be delivered directly into the lower intestine. As it was found that most patients responded successfully to oral yoghurt therapy alone, intubation was discontinued.

We found yoghurts to be a safe and efficient means of administering PR88. Viable counts were about 10^8/ml so one yoghurt contained 10^{10} bacteria. The yoghurt pH was about 4.5 so this reduced the risks of contamination; pathogens such as salmonella and listeria are not able to survive at low pHs. PR88 survived well in the acid yoghurt environment and the yoghurt-grown bacteria were in a suitable metabolic state to colonise the gut.

The patients suffering from IBS who were involved in this trial were severe, chronic cases with whom all conventional other types of therapy had failed. Most of them had suffered from IBS for 10-20 years and so were most unlikely to recover spontaneously during our test period. Similarly although IBS symptoms can be influenced by psychological factors previous types of therapy had not induced a 'psychological cure' in these patients. PR88 therapy was tested on long term, well understood IBS patients and the improvements in their condition and quality of life were genuine.

Table 1

Summary of IBS Patients treated with Ent.Faecium PR88			
A. High volume diarrhoea cases			
Patient	length of time with IBS (years)	Date commenced probiotic therapy	
		i/c tube, then yoghurt,	oral yoghurt only
1.	10	6/88*	-
2.	12	4/89	-
3.	20	9/89	-
4.	Not Known	-	12/89
5.	7	3/90	-
6.	10	-	6/90
7.	10	3/90	-
8.	Not Known	10/90	-
9.	Not Known	6/90	-
B. Others			
Patient	Length of time with IBS (years)	Date commenced probiotic therapy	
		ic/tube, then yoghurt,	oral yoghurt only
10.**	2	-	3/90
11.**	5	2/90	-
12.**	10	8/90	-
13.	Not Known	2/90	-
14.	20	7/90	-
15.	Not Known	-	6/90
16.	Not Known	-	6/90
17.	Not Known	1/90	-

* initially intubation only

** intermittent diarrhoea.

Table 2

Summary of IBS Patients treated with Ent.Faecium PR88

A. High volume diarrhoea cases

Patient	Reported improvement after yoghurt therapy	Viable count/gm faeces of PR88 after treatment
1.	+	10^5 - 10^9
2.	+	10^7 - ND (normalisation of gut flora)
3.	+	10^5 - 10^9
4.	+	10^5 - 10^8
5.	+	10^7 - 10^8
6.	+	10^6 - 10^8
7.	+	10^6 - 10^8
8.	- lactose intolerant	10^5
9.	- lactose intolerant	10^8 - 10^9

B. Others

Patient	Reported improvement after yoghurt therapy	Viable count/gm faeces of PR88 after treatment
10.*	+	$10^6 - 10^8$
11.*	+	$10^7 - 10^8$
12.*	+	$10^8 - 10^9$
13.	+	$10^7 - 10^9$
14.	+	10^8
15.	-	$10^6 - 10^9$
16.	-	$10^7 - 10^9$
17.	-	10^8

* intermittent diarrhoea

None of the above had Ent.faecium before treatment

Table 3

The average daily faecal weights of the patients before and after probiotic treatment

Patient/dates	Average daily faecal weight	PR88/g.faeces	Comments
Patient 1			
21-23/9/88	3080	ND	Food intol.breakdown
18/10/88	250	2 x 10^6	After intubation.
7-9/6/89	3643	ND	Antibiotic breakdown
19/6/89	200	8 x 10^7	After intubation/yoghurt
24-27/2/90	2096	ND	Antibiotic breakdown

Table 3 (continued)

The average daily faecal weights of the patients before and after probiotic treatment			
Patient/dates	Average daily faecal weight	PR88/g.faeces	Comments
Patient 1			
6-8/3/90	125	3×10^9	After yoghurt.
Patient 2			
7-9/3/90	1398	ND	Pretreatment
24-26/4/89	0	1×10^7	After intubation.
Patient 3			
19-27/6/89	478	ND	Pretreatment
25-27/9/89	208	5×10^7	After intubation/yoghurts
Patient 4			
25-28/11/89	309	ND	Pretreatment
20-22/2/90	148	2×10^9	After yoghurts (never intubated).
Patient 5			
10-13/3/90	590	ND	Pretreatment
3-6/4/90	329	1×10^7	After intubation/yoghurts.
Patient 6			
15-17/5/90	367	ND	Pretreatment
19-21/6/90	128	4×10^8	After nasopharyngeal tube, then yoghurts
Patient 7			
24-27/2/90	548	ND	Pretreatment
13-16/5/90	123	2×10^7	After intubation/yoghurt.
ND = not detected			

Table 4

Irritable Bowel Syndrome - patients symptoms index

Determination based on 'Simple index' method of Harvey and Bradshaw (1980). The index is based on the number of stools per day plus other symptoms graded 0=very well, 1=slightly below par, 2=poor, 3=very poor, 4=terrible.

	Pre treatment	Post treatment
Patient 1		
Stools per day	20	1
Abdominal pain	3	1
Joint swelling & pain	2	1
	25	3
Patient 2		
Stools per day	5	1
Headache	1	0
	6	1
Patient 3		
Stools per day	4	1
Abdominal pain	2	1
Headache	2	0
Bloating	1	1
	9	3
Patient 4		
Not done		
Patient 5		
Stools per day	10	2
Abdominal pain	1	0
Joint swelling and pain	2	0
Bloating	3	1
	16	3
Patient 6		
Stools per day	4	2
Wind	2	1
	6	3

Patient 7		
Stools per day	5	1
Abdominal pain	3	1
Bloating	3	1
	11	3
Patient 8		
Stools per day	6	7
Abdominal pain	2	2
	8	9
Patient 9		
Stools per day	5	3
Abdominal pain	3	2
Bloating	2	3
	10	8
Patient 10		
Stools per day	3	1
Headache	1	0
Bloating	1	0
	5	1
Patient 11		
Stools per day	3	1
Abdominal pain	3	0
Headache	3	2
Bloating	3	0
	12	3
Patient 12		
Stools per day	8	3
Abdominal pain	2	0
	10	3
Patient 13		
Stools per day	3	2
Joint swelling and pain	3	1
Headache	2	0
	8	3
Patient 14		
Stools per day	3	1
Abdominal pain	3	0
Headache	3	0
Joint swelling and pain	2	1
	11	2

Table 5

Symptom index summary		
Patient	Pre-treatment	Post-treatment
1	25	3
2	6	1
3	9	3
4	Not done	
5	16	3
6	6	3
7	11	3
8	8	9
9	10	8
10	5	1
11	12	3
12	10	3
13	8	3
14	11	2

Example 1

Simultaneous administration to a human patient suffering from IBS, of strain PR88 and a second strain of Enterococcus faecium, having apparently identical biochemical and cultural characteristics (identified as PR192), in a single dose, comprising $1x10^{11}$ PR88 and $1x10^{11}$ PR192, showed that whereas the faecal excretion of strain PR88 persisted at a level of in excess of $1x10^5$ per gram wet weight, for over 50 days post-treatment, the excretion of PR192 persisted at a similar level for less than 5 days post-treatment. Furthermore, the patient experienced a reduction in the symptoms of IBS consistent with at least a partial remission, commencing 7 days after treatment and lasting for more than 50 days.

Example 2

Daily oral administration to a human patient suffering from IBS, of a dose of $1x10^{10}$ Enterococcus faecium PR88, for a continuous period of 14 days resulted in a daily faecal excretion of the organism in excess of $1x10^5$ throughout the period of treatment. This was accompanied by an amelioration of the symptoms of IBS, consistent with at least a partial remission of the condition.

Example 3

Daily oral administration to a human patient suffering from IBS of a dose of $1x10^{10}$ of Enterococcus faecium PR192, (see Example 1), for a continuous period of 7 days although ensuring a faecal excretion of the organism in excess of $1x10^5$ per gram wet weight failed to elicit any amelioration of the symptoms of IBS, consistent with remission. The treatment with PR192 was discontinued due to the continued deterioration in the patient's condition. Treatment with PR88 was substituted and resulted in a beneficial response.

Example 4

A human patient having a naturally-occurring strain of Enterococcus faecium, having identical biochemical and cultural characteristics as PR88 and having a faecal excretion rate of the strain in excess of $1x10^5$ per day, presented with the symptoms of IBS. Administration of a daily oral dose of $1x10^{10}$ of Enterococcus faecium PR88 for a period of 14 days resulted in a daily faecal excretion of strain PR88 in excess of $1x10^5$ organisms per gram and an amelioration of the symptoms consistent with at least a partial remission.

These examples indicate that Enterococcus faecium strain PR88 confers a unique benefit in terms of amelioration of the symptoms of IBS consistent with at least a partial remission, not conferred by other strains of Enterococcus faecium, whether occurring naturally or administered medicinally.

Example 5

Enterococcus faecium strain PR88 was maintained in vials frozen in liquid nitrogen. An inoculum for commercial scale production was propagated from frozen vials in a medium consisting of hydrolysed soy protein, yeast extract, glucose, and buffering salts (eg monopotassium hydrogen phosphate and disodium hydrogen phosphate) and a mineral source (eg magnesium sulphate).

For a commercial scale fermentation, a medium consisting of at least one nitrogen source (eg non-fat dry milk, hydrolyzed soy protein, corn steep liquor and yeast extract) is used, with a carbon and energy source (eg glucose or lactose). A mineral source (eg magnesium sulphate) is included to satisfy requirements for kinase reactions. Buffering salts (eg. monopotassium hydrogen phosphate and disodium hydrogen phosphate) are included to prevent acid injury and promote enhanced viable cell recover. The ingredients are uniformly blended in water and sterilized in a pressurized fermenter vessel. The vessel has aseptic attachments for monitoring and controlling temperature and pH. Immediately after exhaustion of the carbon source(s) or just before complete exhaustion, the vessel is cooled to refrigeration temperature, and the cells are harvested by either centriguation or ultrafiltration.

The cold cell concentrate can either be frozen after the addition of cryoprotectants such as sterile milk, lactose or sucrose solution, glycerol, or monosodium glutamate, or frozen as shallow layers in sterile trays and freeze-dried.

In a typical fermentation, a medium consisting of non-fat dry milk at 1%, yeast extract at 1%, lactose or glucose at 2-3%, magnesium sulfate at 0.1%, and a combination of sodium phosphate and potassium phosphate at 0.9% was used. The sterilized medium had an initial pH between 6.3-6.6. Incubation was at 37°C. The pH stat was set at 5.8. After 14-15 hours the cells were harvested by centrifugation to obtain 10 x concentration. A cryoprotective mixture of milk and lactose was added to the concentrate before lyophilization. A count of 1.5×10^{11} colony forming units per gram of the cell powder was obtained.

Example 6

Enterococcus faecium strain PR88, prepared as a cell powder in accordance with Example 5, is added by simple admixture to a conventional fermented milk product, eg yoghurt, in an amount sufficient to provide amout 10^9 viable PR88 organisms per 100 gm of product. Probiotic benefits are derived by a human consuming the product on a regular basis, consistent with normal levels of consumption of such products.

Example 7

Enterococcus faecium strain PR88 is added to a beverage product in an amount sufficient to provide about 10^9 viable PR88 organisms per 100 ml of product. The beverage is essentially aqueous, but may contain protein, e.g. cadein or soy, plus minerals and electrolytes.

In general, the probiotic organisms of the invention, especially strain PR88, will be used in medicaments, prophylactics and foodstuffs generally as essentially pure cultures.

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Claims

1. Organisms of Enterococcus faecium selected from the group consisting of strain NCIMB 40371 and its Irritable Bowel Syndrome-alleviating mutants and derivatives thereof.

2. Enterococcus faecium strain NCIMB 40371.

3. Organisms of claim 1 or 2 in viable form.

4. Organisms of claim 1 or 2 in lyophilised form.

5. An edible capsule containing organisms according to claim 1 to 4.

6. An edible composition comprising organisms of claim 1 to 4, in a carrier material.

7. A composition according to claim 6, packaged with instructions recommending a mode of administration to a human patient exhibiting symptoms of gastroenteric disorder.

8. A composition according to any of claims 6 or 7, wherein the disorder is Irritable Bowel Syndrome.

9. A composition according to any of claims 6 to 8, being a fermented milk product.

10. A composition according to any of claims 6 to 8, being a spread or dressing.

11. A composition according to any of claims 6 to 8, being a beverage.

12. A composition according to any one of claims 6 to 11, comprising per gramme at least 10^3 viable organisms.

13. A composition according to any one of claims 6 to 12, comprising per gramme at least 10^6 viable organisms.

14. A composition according to any one of claims 6 to 13, comprising per gramme from 10^9 to 10^{10} viable organisms.

15. A composition comprising killed cultures of the organisms according to claim 1 or 2.

16. Animal feed comprising organisms according to any of claims 1 to 4.

17. A process for the preparation of a composition, comprising the step of adding to edible material organisms according to any of claims 1 to 4, in an amount sufficient to provide at least 10^3 organisms per gramme of the composition.

18. Organisms according to any of claims 1 to 4 for use as a medicament.

19. Use of organisms according to any of claims 1 to 4 in the manufacture of a composition for administration to a human patient exhibiting symptoms of gastroenteric disorder.

20. Use according to claim 19, wherein the gasteroenteric disorder is Irritable Bowel Syndrome.

21. Use according to claim 19, wherein the gasteroenteric disorder is travellers diarrhoea.

22. Use of organisms according to any of claims 1 to 4 in the manufacture of a composition for administration to animals.

Patentansprüche

1. Organismen von Enterococcus faecium, ausgewählt aus der aus Stamm NCIMB 40371, seinen Reizdarmsyndrom-lindernden Mutanten und Abkömmlingen davon bestehenden Gruppe.

2. Enterococcus faecium Stamm NCIMB 40371.

3. Organismen nach Anspruch 1 oder 2 in lebensfähiger Form.

4. Organismen nach Anspruch 1 oder 2 in lyophilisierter Form.

5. Eßbare Kapsel, enthaltend Mikroorganismen nach einem der Ansprüche 1 bis 4.

6. Eßbare Zusammensetzung, umfassend Organismen nach einem der Ansprüche 1 bis 4 in einem Trägermaterial.

7. Zusammensetzung nach Anspruch 6, verpackt mit Anweisungen, die einen Modus der Verabreichung an einen Symptome gastroenterischer Störung aufweisenden Humanpatienten empfehlen.

8. Zusammensetzung nach einem der Ansprüche 6 oder 7, wobei die Störung Reizdarmsyndrom ist.

9. Zusammensetzung nach einem der Ansprüche 6 bis 8, wobei es sich um ein fermentiertes Milchprodukt handelt.

10. Zusammensetzung nach einem der Ansprüche 6 bis 8, wobei es sich um einen Brotaufstrich oder um ein Dressing handelt.

11. Zusammensetzung nach einem der Ansprüche 6 bis 8, wobei es sich um ein Getränk handelt.

12. Zusammensetzung nach einem der Ansprüche 6 bis 11, die pro Gramm mindestens 10^3 lebensfähige Organismen umfaßt.

13. Zusammensetzung nach einem der Ansprüche 6 bis 12, die pro Gramm mindestens 10^6 lebensfähige Organismen umfaßt.

14. Zusammensetzung nach einem der Ansprüche 6 bis 13, die pro Gramm 10^9 bis 10^{10} lebensfähige Organismen umfaßt.

15. Zusammensetzung, die abgetötete Kulturen der Organismen nach Anspruch 1 oder 2 umfaßt.

16. Tiernahrung, die Organismen nach einem der Ansprüche 1 bis 4 umfaßt.

17. Verfahren zur Herstellung einer Zusammensetzung, umfassend den Schritt der Zugabe von Organismen nach einem der Ansprüche 1 bis 4 zu eßbarem Material in einer Menge, die zur Bereitstellung von mindestens 10^3 Organismen pro Gramm der Zusammensetzung ausreicht.

18. Organismen nach einem der Ansprüche 1 bis 4 zur Verwendung als Medikament.

19. Verwendung der Organismen nach einem der Ansprüche 1 bis 4 zur Herstellung einer Zusammensetzung zur Verabreichung an einen Humanpatienten, der Symptome gastroenterischer Störung aufweist.

20. Verwendung nach Anspruch 19, wobei die gastroenterische Störung das Reizdarmsyndrom ist.

21. Verwendung nach Anspruch 19, wobei die gastroenterische Störung Reise-Diarrhöe ist.

22. Verwendung von Organismen nach einem der Ansprüche 1 bis 4 bei der Herstellung einer Zusammensetzung zur Verabreichung an Tiere.

Revendications

1. Organismes de Enterococcus faecium sélectionnés à partir du groupe formé la souche NCIMB 40371 et ses mutants soulageant le syndrome du colon irritable et ses dérivés.

2. Enterococcus faecium souche NCIMB 40371.

3. Organismes selon les revendications 1 ou 2 sous forme viable.

4. Organismes selon les revendications 1 ou 2 sous forme lyophilisée.

5. Gélule comestible contenant les organismes selon les revendications 1 à 4.

6. Composition comestible comprenant les organismes selon les revendications 1 à 4, dans un matériau véhicule.

7. Composition selon la revendication 6, emballée avec les instructions recommandant un mode d'administration à un patient humain présentant des symptômes de trouble gastroentérique.

8. Composition selon l'une quelconque des revendications 6 ou 7, dans laquelle le trouble est le syndrome du colon irritable.

9. Composition selon l'une quelconque des revendications 6 à 8, étant un produit lacté fermenté.

10. Composition selon l'une quelconque des revendications 6 à 8, étant une pâte à tartiner ou un nappage.

11. Composition selon l'une quelconque des revendications 6 à 8, étant une boisson.

12. Composition selon l'une quelconque des revendications 6 à 11, comprenant par gramme au moins 10^3 organismes viables.

13. Composition selon l'une quelconque des revendications 6 à 12, comprenant par gramme au moins 10^6 organismes viables.

14. Composition selon l'une quelconque des revendications 6 à 13, comprenant par gramme de 10^9 à 10^{10} organismes viables.

15. Composition comprenant des cultures tuées des organismes selon la revendication 1 ou 2.

16. Alimentation animale comprenant des organismes selon l'une quelconque des revendications 1 à 4.

17. Procédé pour la préparation d'une composition, comprenant l'étape consistant à ajouter à un matériau comestible des organismes selon l'une quelconque des revendications 1 à 4, en une quantité suffisante pour fournir au moins 10^3 organismes par gramme de la composition.

18. Organisme selon l'une quelconque des revendications 1 à 4 pour une utilisation en tant que médicament.

19. Utilisation d'organismes selon l'une quelconque des revendications 1 à 4, dans la fabrication d'une composition pour une administration à un patient humain présentant des symptômes de trouble gastroentérique.

20. Utilisation selon la revendication 19, dans laquelle le trouble gastroentérique est le syndrome du colon irritable.

21. Utilisation selon la revendication 19, dans laquelle le trouble gastroentérique est la diarrhée du voyageur.

22. Utilisation d'organismes selon l'une quelconque des revendications 1 à 4, dans la fabrication d'une composition pour une administration aux animaux.